CONFIRMATION OF THE SAFETY OF AUTOLOGOUS BLOOD DONATION BY PATIENTS AWAITING HEART OR LUNG TRANSPLANTATION

A controlled study using hemodynamic monitoring

Background: **Though earlier investigations have demonstrated the efficacy of autologous blood transfusion in reducing allogeneic blood exposure in patients undergoing heart or lung transplantation, questions remain regarding the safety of blood donation by patients with severe heart or lung disease.** *Methods:* **Response to autologous blood donation by candidates for heart and lung transplantation and a group of age- and gender-matched control subjects was studied. Heart rate, blood pressure, oxygen saturation, and cardiac rhythm were examined before and after phlebotomy, and response to orthostatic challenge was evaluated. Patients were also questioned regarding impressions of changes in subjective sense of well being. Differences between patients and control subjects were evaluated by the paired *t* test and Fisher's exact test. An alpha of 0.05 was used in all testing to determine statistical significance.** *Results:* **Eighteen candidates for heart transplantation, 16 candidates for lung transplantation, and their matched control subjects were studied. Though patients and control subjects differed with respect to baseline hemodynamic measurements, significant differences between the groups' responses to phlebotomy were not observed. After whole blood donation, orthostatic challenge resulted in a mean change in mean arterial pressure of −2.1 mm Hg in candidates for heart transplantation compared with a mean of +3.6 mm Hg in their control subjects ($p = 0.062$). In candidates for lung transplantation there was a mean change of +2.2 mm Hg after orthostatic challenge versus a mean change of +8.5 mm Hg in their control subjects ($p = 0.052$). Furthermore, no changes in cardiac rhythm or arterial oxygen saturation were detected.** *Conclusions:* **The hemodynamic effects of autologous blood donation in a group of patients with significant cardiac or pulmonary disease were not different from those observed in patients considered acceptable candidates for autologous blood collection. On the basis of these objective findings, we believe that patients with less severe degrees of heart or lung disease should not be excluded from participation in autologous blood donation programs.**
(J THORAC CARDIOVASC SURG 1995;110:1594-9)

E. Klapper, MD, S. H. Pepkowitz, MD, L. Czer, MD, C. Inducil, RN, L. Scott, RN, and D. Goldfinger, MD, *Los Angeles, Calif.*

From the Rita and Taft Schreiber Division of Transfusion Medicine (Department of Pathology and Laboratory Medicine) and the Department of Cardiothoracic Surgery, Cedars-Sinai Medical Center, Los Angeles, Calif.

Supported by a grant from the Rita and Taft Schreiber Foundation.

Received for publication Nov. 14, 1994.

Accepted for publication April 11, 1995.

Address for reprints: Ellen Klapper, MD, Associate Director, Rita and Taft Schreiber Division of Transfusion Medicine, Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, 8700 Beverly Blvd., Room 3728, Los Angeles, CA 90048.

0022-5223/95 $5.00 + 0 **12/1/65539**

Autologous blood predeposit and transfusion have been effectively used as alternatives to allogeneic blood transfusion for many years. The recent growth in popularity of this procedure, related directly to heightened awareness of the risks of allogeneic blood exposure, has forced the medical community to address issues of safety and utility of autologous blood collection in groups of patients commonly considered too ill to donate their own blood. Although some investigators have expressed concern about the safety of blood donation for many patients with underlying medical illnesses, these reservations have not been based on controlled studies revealing any demonstrable dangers for such categories of

patients. Furthermore, results of our studies[1] and those of other investigators[2, 3] have suggested that many autologous blood programs practice overly restrictive policies in deciding whether to allow patients with significant medical abnormalities to donate their blood for subsequent surgical procedures. This is particularly true when patients with significant cardiac or pulmonary disease are considered.

Recently, Spiess and coworkers[4] reported the results of their studies of hemodynamic changes in a group of autologous blood donors who were considered to be at high risk for complications from autologous blood donation. The majority of these patients had a variety of cardiovascular abnormalities. Although their studies revealed various hemodynamic alterations after blood donation, none of their patients demonstrated significant clinical evidence of adverse effects of the blood donation process. Furthermore, control patients used for this study consisted of healthy medical residents rather than age- and gender-matched subjects without known cardiovascular disease.

More recently, we reported our experience in collecting autologous blood from patients with end-stage heart or lung disease awaiting organ transplantation.[5] We demonstrated that such donations were efficacious in eliminating or reducing allogeneic blood exposure associated with the subsequent transplant operations. More important, the safety of autologous blood donation was suggested by a lack of clinically significant adverse reactions in this group of seriously ill patients.

To prove the safety of autologous blood donation for patients with extreme compromise of cardiac or pulmonary function, we expanded the scope of our studies to include more objective measurements of cardiac and pulmonary responses to the blood donation process. This group of candidates for heart and lung transplantation was chosen for study to provide a model of patients with significant compromise of cardiovascular or pulmonary function. Few blood collection centers will routinely encounter candidates for heart and lung transplantation; however, the findings of this study can be applied to patients with less severe cardiopulmonary disease when their eligibility for autologous blood donation is considered. In addition, we investigated an age- and gender-matched control population without known cardiac or pulmonary disease to ascertain their responses to autologous blood donation. These latter patients were considered to be at low risk for phlebotomy-associated complications. For these studies we used a battery of noninvasive assessments of cardiorespiratory function before, during, and after phlebotomy.

Patients and methods

All patients accepted as heart or lung transplant candidates were considered potential study participants. Eighteen candidates for heart transplantation and 16 candidates for lung transplantation were studied. Patients were evaluated before each donation to determine eligibility. Exclusion criteria were hematocrit value less than 33%, systolic blood pressure less than 90 or greater than 200 mm Hg, diastolic blood pressure less than 60 or greater than 100 mm Hg or heart rate less than 55 or more than 120 beats/min. Patients with cardiac arrhythmias (other than ventricular tachycardia) or with congestive heart failure (unless they had acute pulmonary edema) who were free of symptoms were eligible for inclusion in the study. Patients who required oxygen at 5 L/min or less by nasal prongs were also permitted to donate. The volume of blood collected ranged from 380 to 450 ml and was dependent on patient weight and hematocrit value. The decision to replace intravascular volume with saline solution or albumin was made jointly by a transfusion medicine physician and a transplant team physician. Only those patients highly dependent on intravascular volume for maintenance of adequate cardiac output received intravenous fluid replacement.

Hemodynamic assessment of the effect of blood donation included measurement of heart rate and blood pressure in the supine, sitting, and standing positions. Pulse oximetry measurements and a continuous electrocardiogram rhythm strip were obtained during and for a 30-minute period after blood donation. All patients were observed for at least 30 minutes after phlebotomy before they were allowed to ambulate. A questionnaire was administered after the blood donation and 24 hours later to evaluate subjective patient response to phlebotomy. The control group of age- and gender-matched autologous blood donors without known heart or lung disease was studied in the same manner. All aspects of this study were reviewed and approved by the Medical Center's institutional review board.

Statistical methods. The paired t test was used to compare baseline characteristics between patients and control subjects. For each group, change from baseline was calculated for the "postdonation" period. The relative magnitude of these changes was compared between groups by the paired t test. Event rates were compared between groups by Fisher's exact test. An alpha of 0.05 was used in all testing to determine statistical significance and all testing was two-sided.

Results

Although patients and control subjects might have donated more than 1 unit of blood in prepa-

Table I. *Age, gender, hematocrit value, and volume replacement*

	Age (yr)			*Hematocrit*		*No. of patients receiving volume replacement*
	Mean	*Range*	*Gender*	*Mean ± SD*	*Range*	
Candidates for heart transplantation (n = 18)	55	36-68	M, 18	41.4% ± 3.2%	36%-48%	6
Control subjects (n = 18)	55	36-68	Matched	41.6% ± 3.2%	37%-50%	0
Candidates for lung transplantation (n = 16)	47.4	27-65	M, 7; F, 9	46.0% ± 7.1%	37%-65%	3
Control subjects (n = 16)	47.6	29-63	Matched	40.1% ± 3.7%	35%-47%	0

M, Male; *F,* female; *SD,* standard deviation.

Table II. *Heart rate measured in supine position*

	Heart rate (beats/min)			
	Predonation (mean ± SE)	*Postdonation (mean ± SE)*	*Mean change (range)*	*p Value*
Candidates for heart transplantation	85.5 ± 2.95	82.8 ± 3.33	−2.7 (+8 to −16)	0.2
Control subjects	65.1 ± 3.17	64.0 ± 3.35	−1.1 (+9 to −10)	
Candidates for lung transplantation	94.9 ± 4.27	89.9 ± 3.69	−5.0 (+5 to −18)	0.3
Control subjects	71.9 ± 2.11	71.3 ± 2.23	−0.6 (+6 to −6)	

SE, Standard error.

ration for the operation, for purposes of statistical analysis only the first donation was used for calculation of the groups' mean responses to phlebotomy. Age, gender, and predonation hematocrit values for patients and control subjects are shown in Table I. Candidates for lung transplantation had diagnoses of primary pulmonary hypertension, pulmonary fibrosis, or emphysema and candidates for heart transplantation had diagnoses of ischemic cardiomyopathy or idiopathic dilated cardiomyopathy.

Volume replacement was provided to the three patients with primary pulmonary hypertension and to six candidates for heart transplantation with right ventricular disease. These patients had severe right-sided heart failure and were thought to be highly dependent on intravascular volume to maintain cardiac output (Table I).

Mean baseline heart rate was higher in the candidates for cardiac transplantation than in the control subjects. Mean heart rate in the supine position was 85.5 beats/min in the patient group versus 65.1 beats/min in the control group ($p < 0.01$). After donation there was little change in mean heart rate measured in the supine position with no significant difference between patients and control subjects in their response to phlebotomy (Table II).

Before phlebotomy, mean heart rate was higher in the group of candidates for lung transplantation when compared with that of their control subjects. In the supine position, the baseline mean heart rate of candidates for transplantation was 94.9 beats/min whereas that of the control subjects was 71.9 beats/min ($p < 0.01$). After blood donation, the mean heart rate of candidates for transplantation decreased to 89.9 beats/min whereas that of control subjects remained essentially unchanged ($p = 0.3$) (Table II).

Baseline mean arterial pressures in candidates for heart transplantation and control subjects were not significantly different and in response to phlebotomy demonstrated little change (Table III). In candidates for lung transplantation, mean arterial pressure before and after phlebotomy was significantly greater than that in their control subjects ($p < 0.05$), but there was no significant difference in their responses to blood donation (Table III).

Responses of heart rate and mean arterial pressure to an orthostatic challenge before and after phlebotomy are shown for patients and control subjects in Tables IV and V. Before blood donation the mean heart rate of candidates for heart transplantation increased 1.4 beats/min, whereas that of control subjects increased 8 beats/min when they were raised from a supine to a standing position ($p = 0.138$) (Table IV). After blood donation, mean heart rate in candidates for heart transplantation and their control subjects increased, with that in control subjects increasing more than that in patients (15.2 versus 3.5 beats/min, $p = 0.0006$) (Table IV).

Table III. *Mean arterial pressure measured in supine position*

	Mean arterial pressure (mm Hg)			
	Predonation (mean ± SE)	*Postdonation (mean ± SE)*	*Mean change (range)*	*p Value*
Candidates for heart transplantation	84.4 ± 2.8	83.5 ± 2.25	−0.9 (+13 to −10)	0.9
Control subjects	92.5 ± 3.17	91.9 ± 3.03	−0.6 (+12 to −12)	
Candidates for lung transplantation	97.5 ± 2.47	94.4 ± 3.15	−3.1 (+18 to −20)	0.9
Control subjects	87.4 ± 3.91	83.9 ± 3.11	−3.5 (+12 to −21)	

SE, Standard error.

Table IV. *Heart rate response to orthostatic challenge*

	Heart rate (beats/min)			
	Supine (mean ± SE)	*Standing (mean ± SE)*	*Change*	*p Value*
Predonation				
Candidates for heart transplantation	85.5 ± 2.85	86.9 ± 3.42	+1.4	0.138
Control subjects	65.1 ± 3.17	73.1 ± 3.15	+8.0	
Candidates for lung transplantation	94.9 ± 4.27	101.7 ± 5.69	+6.8	0.745
Control subjects	71.9 ± 2.11	78.0 ± 2.86	+6.1	
Postdonation				
Candidates for heart transplantation	82.8 ± 3.33	86.3 ± 4.14	+3.5	0.0006
Control subjects	64.9 ± 3.35	80.1 ± 3.75	+15.2	
Candidates for lung transplantation	89.9 ± 3.69	102.0 ± 5.66	+12.1	0.288
Control subjects	71.3 ± 2.23	88.0 ± 3.60	+16.7	

SE, Standard error.

Table V. *Mean arterial pressure response to orthostatic challenge*

	Mean arterial pressure (mm Hg)			
	Supine (mean ± SE)	*Standing (mean ± SE)*	*Change*	*p Value*
Predonation				
Candidates for heart transplantation	84.3 ± 2.80	82.2 ± 2.75	−2.1	0.011
Control subjects	92.5 ± 3.17	95.8 ± 3.28	+3.3	
Candidates for lung transplantation	97.5 ± 2.47	96.3 ± 2.91	−1.2	0.016
Control subjects	87.4 ± 3.91	93.2 ± 3.90	+5.8	
Postdonation				
Candidates for heart transplantation	83.5 ± 3.33	81.2 ± 3.18	−2.3	0.062
Control subjects	91.9 ± 3.03	95.5 ± 3.35	+3.6	
Candidates for lung transplantation	94.4 ± 3.15	96.6 ± 2.23	+2.2	0.052
Control subjects	83.9 ± 3.11	92.4 ± 4.55	+8.5	

SE, Standard error.

Before donation, mean arterial pressure exhibited small changes in candidates for heart transplantation and control subjects when donors were subjected to an orthostatic challenge. After donation, similar changes were observed (Table V).

Candidates for lung transplantation and control subjects had similar increases in heart rate when they were raised from a supine to standing position before phlebotomy. After blood donation, the mean heart rate of patients and control subjects increased similarly (Table IV).

Before donation, candidates for lung transplantation and control subjects differed in mean arterial pressure response to an orthostatic challenge. Mean arterial pressure in patients remained essentially unchanged, whereas mean arterial pressure in the control group increased slightly ($p = 0.016$) (Table V). Postdonation mean arterial pressure increased in both candidates for lung transplantation and control subjects, but more so in the control group ($p = 0.052$) (Table V).

Oxygen saturation values for candidates for transplant and control subjects are shown in Table VI. Values in candidates for lung transplantation dif-

Table VI. *Arterial oxygen saturation*

	Arterial oxygenation saturation (%)			
	Predonation (mean ± SE)	*Postdonation (mean ± SE)*	*Change (mean ± SE)*	*p Value*
Candidates for heart transplantation	96.8 ± 0.4	97.2 ± 0.4	+0.4 ± 0.4	0.6
Control subjects	96.9 ± 0.5	97.6 ± 0.3	+0.7 ± 0.3	
Candidates for lung transplantation	95.3 ± 0.9	95.9 ± 0.8	+0.6 ± 0.5	0.3
Control subjects	98.6 ± 0.4	98.6 ± 0.3	0 ± 0.2	

SE, Standard error.

Table VII. *Number of untoward responses elicited by postphlebotomy questionnaire*

	Immediately postdonation	*p Value*	*During 24 hr postdonation*	*p Value*
Candidates for heart transplantation	5* (28%)	0.045	1† (5%)	1.00
Control subjects	0 (0%)		0 (0%)	
Candidates for lung transplantation	1‡ (6%)	1.00	2§ (13%)	1.00
Control subjects	2§ (13%)		3§ (18%)	

*Transient lightheadedness in four patients; mild transient diaphoresis in one patient.

†Transient lightheadedness.

‡Mild fatigue.

§Mild fatigue or transient lightheadedness.

fered from those in control subjects both before and after phlebotomy ($p < 0.05$) and no change in oxygen saturation was observed after the blood donation. No differences in oxygen saturation were observed between candidates for heart transplantation and control subjects before or after phlebotomy. No new cardiac arrhythmias were noted on electrocardiogram in any patients or control subjects in either of the two study groups.

Donor responses to a series of questions were actively solicited immediately after and 24 hours after phlebotomy (Table VII). The intent was to elicit any subtle subjective change in well-being that was not observed. With the exception of one candidate for heart transplantation who had mild diaphoresis after donation, no donor had a donor reaction characterized by increased vagal tone. A mild, transient sensation of lightheadedness was the most common response, and no patient required treatment for any adverse event after donation.

Discussion

The data collected in this study provide important new information regarding the hemodynamic response to blood donation by patients with severe cardiac or pulmonary disease. Because control subjects were matched for age and gender, it was possible to compare accurately the study groups' responses to phlebotomy with those of patients currently thought to be medically eligible for autologous blood donation. Although the two populations of patients differed significantly in baseline hemodynamic characteristics, their responses to phlebotomy were essentially similar. Although some differences in measured parameters between patients and control subjects reached statistical significance, in all instances the magnitude of difference was clinically insignificant. Neither group demonstrated significant hemodynamic compromise as a result of blood donation.

Interestingly, control patients in our study had a significantly different increase in heart rate when they were raised to the standing position after phlebotomy compared with that in patients with cardiopulmonary disease. This may have been related to the study patients' underlying cardiovascular abnormalities and to the effects of drug therapy they were receiving, which may have prevented increases in heart rate in response to orthostatic challenge. However, neither group encountered significant reduction in blood pressure from orthostatic challenge after blood donation. Most important, no donor had significant clinical consequences of phlebotomy.

When questioned, candidates for heart transplantation reported a negative subjective impression after phlebotomy more frequently than did their control subjects ($p = 0.045$). However, these symptoms of lightheadedness or diaphoresis were mild and transient. No patient was deferred from further

participation in the autologous blood predeposit study as the result of a poor response to prior blood donation. Twenty-four hours after donation, no difference in adverse response rate could be detected. For the group of candidates for lung transplantation and their control subjects, subjective response to blood donation was similar.

The report of Spiess and coworkers[4] has raised concern that patients with cardiovascular disease might be at increased risk for hemodynamic compromise after autologous blood donation. Our studies indicate that such patients' responses do not significantly differ from those of patients considered to be acceptable autologous blood donors as ascertained by hemodynamic measurements before and after the blood donation process. The fact that our patients had less severe alteration in blood pressure after blood donation than those in the report by Spiess and co-workers[4] may relate to the fact that none of our patients was allowed to ambulate for at least 30 minutes after the blood donation process. It is reasonable that patients with a history of cardiopulmonary disease might require an increased recovery period after the blood donation process before being allowed to ambulate. Most important, we believe that our data and those presented by Spiess and coworkers[4] demonstrate that patients with severe cardiopulmonary dysfunction do not have significant clinical complications after the blood donation process.

Though we encountered no dangerous reactions, patients awaiting organ transplantation are best cared for in a hospital blood donor facility, where full medical support is available. For this study, we chose patients with the most extreme degree of heart or lung disease to serve as a model for autologous donation that may reasonably be applied to the much larger population of patients with less severe disease who may go to a blood center for collection of autologous blood. Certainly the fact that our patients with the most severe degrees of cardiopulmonary compromise were found to participate in autologous blood donation without significant clinical response indicates that those patients with less severe degrees of cardiopulmonary disease can easily tolerate the stress of autologous blood donation without significant concern.

Although some of our patients were given volume replacement with saline solution or albumin after blood donation, no attempt was made to study the need for volume replacement or the lack thereof. Only those patients with severe right-sided heart failure were preselected to receive volume replacement. Evaluation of the necessity or possible benefit of this procedure was beyond the scope of this study. However, it should be noted that patients with extremely severe cardiac compromise (without right-sided failure) tolerated blood donation without adverse effects in the absence of volume replacement. Therefore we believe that volume replacement is probably unnecessary for the vast majority of patients with cardiac disease who might be considered for autologous blood donation.

The size of our study population poses the potential that a relatively small risk from blood donation might not have been detected for patients with severe cardiopulmonary compromise. However, the known risks of allogeneic blood transfusions are real and suggest that a small risk that might accompany autologous blood donation might be tolerable in an effort to spare patients the complications of allogeneic blood transfusions. Though advancements in donor screening and laboratory testing of donated blood have increased the safety of transfusion therapy, we must heed the lessons learned during the past 15 years. No one could have anticipated the spread of human immunodeficiency virus by blood transfusion. Therefore we believe that these findings provide strong reasons to allow patients with known cardiovascular or pulmonary disease to participate in autologous blood donation programs so as to minimize their exposure to allogeneic transfusion and the potential complications associated with such therapy.

REFERENCES

1. Mann M, Sacks HJ, Goldfinger D. Safety of autologous blood donation prior to elective surgery for a variety of potentially "high-risk" patients. Transfusion 1983;23: 229-32.
2. AuBuchon JP, Popovsky MA. The safety of preoperative autologous blood donation in the non-hospital setting. Transfusion 1991;31:513-7.
3. Owings DV, Kruskall MS, Thurer RL, Donovan LM. Autologous blood donations prior to elective cardiac surgery: safety and effect on subsequent blood use. JAMA 1989;262:1963-8.
4. Spiess BD, Sassetti R, McCarthy RJ, Narbone RF, Tuman KJ, Ivankovich AD. Autologous blood donation: hemodynamics in a high-risk patient population. Transfusion 1992;32:17-22.
5. Goldfinger D, Capon S, Czer L, et al. Safety and efficacy of preoperative donation of blood for autologous use by patients with end-stage heart or lung disease who are awaiting organ transplantation. Transfusion 1993;33:336-40.